PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

OHNO, Seiji
Ohno & Partners
Kasumigaseki Building 36F
3-chome
Chiyoda-ku, Tokyo 1006036
JAPON

Date of mailing *(day/month/year)* 03 August 2006 (03.08.2006)	
Applicant's or agent's file reference PGK-9001WO	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2004/016805	International filing date *(day/month/year)* 05 November 2004 (05.11.2004)
Applicant JAPANESE FOUNDATION FOR CANCER RESEARCH et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
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ATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference PGK-9001WO	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2004/016805	International filing date *(day/month/year)* 05 November 2004 (05.11.2004)	Priority date *(day/month/year)* 05 November 2003 (05.11.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant JAPANESE FOUNDATION FOR CANCER RESEARCH		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 27 July 2006 (27.07.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yoshiko Kuwahara e-mail: pt07@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference PGK-9001WO	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/016805	05.11.2004	05.11.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant
JAPANESE FOUNDATION FOR CANCER RESEARCH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016805

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☒ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☒ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016805

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

☐ paid additional fees

☐ paid additional fees under protest

☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with

☒ not complied with for the following reasons:

The technical feature common to claims 1-16 relates to a method of predicting risk of onset of granulocytopenia due to paclitaxel therapy by identifying polymorphisms at polymorphism sites in CYP2C8 gene or BUBlb gene, but the fact that sensitivity of a patient to paclitaxel therapy can be predicted by identifying polymorphisms at polymorphism sites in CYP2C8 gene, as reported in "Biol. Pharm. Bull., 2001, Vol. 24, No. 12, pp. 1427-1430" and "Biochemical Pharmacology, 2002, Vol. 64, pp. 1579-1589," and elsewhere was already known, and thus this common technical feature cannot be found to be a special technical feature.

Accordingly, there is no technical relationship involving special technical features among the inventions in claims 1-16 and these inventions cannot be found to be so linked as to form a single general inventive concept.

Consequently, the inventions described in the claims of the present application include the following six inventions:

(1) parts relating to identification of a gene polymorphism at the 11th base in the sequence of CYP2C8 gene specified by SEQ ID NO:1 in claims 1-3, 6, 10-12 and 14-15;

(2) parts relating to identification of a gene polymorphism at the 11th base in the sequence of CYP2C8 gene specified by SEQ ID NO:2 in claims 1-3, 6, 10-12 and 14-15;

(3) parts relating to identification of a gene polymorphism at the 11th base in the sequence of CYP2C8 gene specified by SEQ 10 NO:3 in claims 1-3, 6, 10-12 and 14-15;

(4) parts relating to identification of a gene polymorphism at the 11th base in the sequence of CYP2C8 gene specified by SEQ ID NO:4 in claims 1-3 and 6-16;

(5) parts relating to identification of a gene polymorphism at the 11th base in the sequence of CYP2CB gene specified by SEQ ID NO:5 in claims 1-3, 6, 10 -12 and 14-15; and

(6) parts relating to identification of a gene polymorphism in BUBlb gene in claims 1 and 6-16 and the inventions in claims 4-5.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

☐ all parts

☒ the parts relating to identification of a gene polymorphism at the 11th base in the sequence of CYP2C8 gene specified by SEQ ID NO:1 in claims 1-3, 6, 10-12 and 14-15

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016805

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-3, 6, 10-12, 14-15	YES
	Claims		NO
Inventive step (IS)	Claims	12, 15	YES
	Claims	1-3, 6, 10-11, 14	NO
Industrial applicability (IA)	Claims	1-3, 6, 10-12, 14-15	YES
	Claims		NO

2. Citations and explanations:

Document 1: JP 2003-93068 A (Director General of the National Institute of Health Sciences) 02 April 2003
Document 2: Biochem Pharmacol, 2002, Vol. 64, No. 11, pp.1579-1589
Document 3: Biol Pharm Bull, 2001, Vol.24, No.12, pp.1427-1430
Document 4: JSNP DATABASE (http://snp.ims.u-tokyo.ac.jp/)
JSNP ID: IMS-JST111898 (11 October 2001)

Claims 1-3, 6, 10-11, and 14

The inventions in claims 1-3, 6, 10-11 and 14 do not appear to involve an inventive step over documents 1-4 cited in the ISR.

Documents 1-3 are found to describe the ability to predict patient sensitivity to paclitaxel therapy by identifying polymorphisms at polymorphism sites in CYP2C8 gene.

In addition, document 4 describes SNP present in SYP2C8 gene region.

As such, the use of SNP described in document 4 as a polymorphism for investigation in methods of predicting patient sensitivity in paclitaxel therapy described in documents 1-3 is not found to pose any exceptional difficulty.

In addition, granulocytopenia is well known to experts in the relevant technical field as a representative side effect of paclitaxel, and thus use of these methods in predicting risk of onset of granulocytopenia is not found to pose any exceptional difficulty.

The adoption of configurations of the inventions described in claims 1-3, 6, 10-11, and 14 is not considered to yield exceptionally striking results.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Claims 12 and 15

The inventions described in claims 12 and 15 appear to possess novelty and involve an inventive step over documents 1-4 cited in the ISR.

The relationship between the BUB1b gene and risk of onset of granulocytopenia due to paclitaxel therapy is not described in any of these documents, nor is it obvious to an expert in the relevant technical field.